**Supplementary table 1.** Clinical characteristics of the type 2 diabetes patients.

|  |  |  |  |
| --- | --- | --- | --- |
| **Traits** | **Type 2 diabetes** | **Type 2 diabetes (30≤ age <60)** | **Type 2 diabetes (age ≥60)** |
| **n=4,036** | **n=2,480** | **n=1,451** |
| **Men** | **Women** | ***P*** | **Men** | **Women** | ***P*** | **Men** | **Women** | ***P*** |
| **Sample size, *n*** | 1,765 | 2,271 |  | 1,111 | 1,369 | ***—*** | 590 | 861 | ***—*** |
| **Age, years** | 53.00 (45.00, 63.00) | 56.00 (49.00, 65.00) | **2.83×10-11** | 49.00 (43.00, 54.00) | 51.00 (45.00, 56.00) | **3.10×10-9** | 67.00 (63.00, 71.00) | 67.00 (63.00, 71.00) | 0.773 |
| **BMI, kg/m2** | 25.90 (23.74, 28.39) | 25.63 (23.29, 28.13) | **0.008** | 26.15 (24.09, 28.63) | 25.60 (23.40, 28.25) | **0.002** | 25.43 (23.13, 27.66) | 25.68 (23.11, 27.99) | 0.718 |
| **WC, cm** | 91.00 (85.00, 97.00) | 86.00 (80.00, 92.00) | **1.88×10-54** | 91.00 (85.00, 98.00) | 85.00 (79.00, 91.00) | **7.36×10-52** | 90.65 (84.00, 96.00) | 87.00 (81.00, 94.00) | **1.09×10-9** |
| **General obesity, *n* (%)** | 495 (28.08%) | 592 (26.17%) | 0.177 | 335 (30.15%) | 368 (26.88%) | 0.072 | 135 (22.88%) | 214 (24.85%) | 0.388 |
| **Abdominal obesity, *n* (%)** | 999 (56.83%) | 1,260 (55.65%) | 0.457 | 1,106 (57.69%) | 1,372 (52.92%) | **0.018** | 331 (56.10%) | 521 (60.65%) | 0.084 |
| **Fasting plasma glucose, mmol/l** | 7.34 (6.25, 8.97) | 7.36 (6.20, 9.00) | 0.685 | 7.43 (6.30, 9.20) | 7.41 (6.24, 9.00) | 0.728 | 7.25 (6.21, 8.63) | 7.27 (6.20, 9.07) | 0.222 |
| **2-h OGTT glucose, mmol/l** | 13.19 (11.21, 16.60) | 13.45 (11.25, 17.30) | 0.076 |  13.04 (11.25, 16.62) |  13.10 (11.10, 17.04) | 0.462 |  13.58 (11.35, 16.74) |  14.03 (11.57, 18.01) | **0.004** |
| **GRS** |  |  |  |  |  |  |  |  |  |
| **Median (IQR)** | 19.00 (18.00, 21.00) | 19.00 (18.00, 21.00) | 0.747 |  19.00 (17.00, 21.00) |  19.00 (18.00, 21.00) | 0.997 |  19.00 (18.00, 21.00) |  19.00 (17.00, 21.00) | 0.639 |
| **NT1(9~18)/NT2(19~20)/NT3(21~27)** | 684/547/534 | 892/700/679 | 0.941 | 428/339/344 | 529/427/413 | 0.896 | 228/189/173 | 347/259/255 | 0.710 |

Abbreviations: BMI, body mass index; GRS, genetic risk score; IQR, interquartile range; OGTT, oral glucose tolerance test; T, tertile; WC, waist circumference.

Data are shown as median (IQR) or %.

*P* values were calculated to assess the intergroup differences using χ2 test or t test. Prior to the t test, all non-Gaussian distributed quantitative traits were natural logarithmically transformed to normalize distributions.

*P* values <0.05 are denoted in bold. *P* values <1.85 × 10-3 which were statistically significant after Bonferroni correction (0.05/27) are denoted in bold and underlined.

**Supplementary table 2.** Information of genotyped single nucleotide polymorphisms.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **SNP** | **Gene** | **Chr.** | **Position****(Build 38)** | **Gene region** | **Major/minor allelea** | **Minor allele frequency** | **PHWE** | **Minor allele frequency in HapMap** | **Related traits** |
|
| **T2D** | **Control** | **T2D** | **Control** | **CEU** | **CHB** |
| rs2568958 | *NEGR1* | 1 | 72299433 | Intergenic | **A**/G | 0.082 | 0.085 | 0.298 | 0.912 | 0.363 | 0.077 | BMI, obesity, weight |
| rs10913469 | *SEC16B* | 1 | 177944384 | Intron | T/**C** | 0.242 | 0.228 | 0.897 | 0.883 | 0.254 | 0.232 | BMI, weight |
| rs2605100 | *SLC30A10* | 1 | 219470882 | Intergenic | **G**/A | 0.220 | 0.228 | 0.119 | 0.659 | 0.314 | 0.182 | Adiposity |
| rs7561317 | *TMEM18* | 2 | 644953 | Intergenic | **G/**A | 0.095 | 0.102 | 0.581 | 0.010 | 0.146 | 0.062 | BMI, weight |
| rs7647305 | *ETV5/DGKG* | 3 | 186116501 | Intergenic | **C**/T | 0.062 | 0.063 | 0.133 | 0.143 | 0.201 | 0.074 | BMI, weight |
| rs10938397 | *GNPDA2* | 4 | 45180510 | Intergenic | A/**G** | 0.322 | 0.296 | 0.071 | 0.868 | 0.451 | 0.250 | BMI, obesity |
| rs2260000 | *BAT2* | 6 | 31625699 | Intron | C/**T** | 0.491 | 0.500 | 0.166 | 0.604 | 0.606 | 0.485 | Weight |
| rs4712652 | *PRL* | 6 | 22078386 | Intron | **A**/G | 0.141 | 0.146 | 0.364 | 0.889 | 0.429 | 0.124 | Adiposity (WHR) |
| rs987237 | *TFAP2B* | 6 | 50835337 | Intron | A/**G** | 0.164 | 0.175 | 0.228 | 0.510 | 0.164 | 0.168 | BMI, adiposity |
| rs545854 | *MSRA* | 8 | 10002570 | Intergenic | **G**/C | 0.416 | 0.419 | 0.035 | 0.189 | 0.177 | 0.348 | WC |
| rs4923461 | *BDNFOS* | 11 | 27635363 | Intron | **A**/G | 0.429 | 0.434 | 0.585 | 0.460 | 0.230 | 0.442 | BMI, weight |
| rs925946 | *BDNF* | 11 | 27645655 | Intergenic | G/**T** | 0.051 | 0.054 | 0.870 | 0.305 | 0.323 | 0.033 | BMI, weight |
| rs10838738 | *MTCH2* | 11 | 47641497 | Intron | A/**G** | 0.329 | 0.313 | 0.187 | 0.968 | 0.363 | 0.307 | BMI |
| rs7138803 | *FAIM2* | 12 | 49853685 | Intergenic | G/**A** | 0.294 | 0.291 | 0.649 | 0.615 | 0.345 | 0.288 | BMI, obesity, weight, WC |
| rs8050136 | *FTO* | 12 | 53782363 | Intron | C/**A** | 0.130 | 0.114 | 0.330 | 0.232 | 0.450 | 0.150 | BMI, Obesity |
| rs1424233 | *MAF* | 16 | 79648854 | Intergenic | **A**/G | 0.323 | 0.322 | 0.886 | 0.058 | 0.442 | 0.307 | Obesity |
| rs12970134 | *MC4R* | 18 | 60217517 | Intergenic | G/**A** | 0.209 | 0.191 | 0.568 | 0.696 | 0.279 | 0.179 | BMI, weight, WC |
| rs1805081 | *NPC1* | 18 | 23560468 | Coding | **A**/G | 0.224 | 0.224 | 0.278 | 0.691 | 0.473 | 0.234 | Obesity |

Abbreviations: SNP, single nucleotide polymorphism; Chr, chromosome; T2D, type 2 diabetes; EU, European; CHB, Han Chinese; BMI, body mass index; WHR, waist-hip-ratio; WC, waist circumference.

a, Risk allele for obesity is denoted in bold and underlined.

**Supplementary table 3.** Associations of single nucleotide polymorphisms with waist circumference and body mass index.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Gene** | **SNP** | **Population** | **Treatment naïve type 2 diabetes****(n=2,555)** | **Type 2 diabetes****(n=4,036)** |
| **WC** | **BMI** | **WC** | **BMI** |
| **β (SE)** | ***P*** | ***P*SNP×sex** | **β (SE)** | ***P*** | ***P*SNP×sex** | **β (SE)** | ***P*** | ***P*SNP×sex** | **β (SE)** | ***P*** | ***P*SNP×sex** |
| ***SLC30A10*** | **rs2605100** | **All** | -0.0063 (0.0037) | 0.093 | 0.802 | -0.0108 (0.0048) | **0.025** | 0.191 | -0.0018 (0.0029) | 0.541 | 0.835 | -0.0049 (0.0037) | 0.186 | 0.211 |
| **Men** | -0.0073 (0.0056) | 0.190 | — | -0.0177 (0.0069) | **0.011** | — | -0.0027 (0.0043) | 0.535 | — | -0.0103 (0.0054) | 0.056 | — |
| **Women** | -0.0057 (0.0050) | 0.251 | — | -0.0053 (0.0066) | 0.418 | — | -0.0015 (0.0039) | 0.697 | — | -0.0010 (0.0051) | 0.847 | — |
| ***TMEM18*** | **rs7561317** | **All** | 0.0128 (0.0052) | **0.015** | 0.310 | 0.0150 (0.0067) | **0.025** | 0.241 | 0.0094 (0.0042) | **0.024** | 0.184 | 0.0092 (0.0053) | 0.084 | 0.256 |
| **Men** | 0.0078 (0.0078) | 0.319 | — | 0.0070 (0.0097) | 0.471 | — | 0.0038 (0.0062) | 0.541 | — | 0.0029 (0.0077) | 0.710 | — |
| **Women** | 0.0165 (0.0070) | **0.018** | — | 0.0213 (0.0092) | **0.021** | — | 0.0139 (0.0056) | **0.013** | — | 0.0143 (0.0073) | 0.051 | — |
| ***GNPDA2*** | **rs10938397** | **All** | 0.0096 (0.0033) | **0.004** | 0.649 | 0.0072 (0.0043) | 0.094 | 0.238 | 0.0078 (0.0026) | **0.002** | 0.292 | 0.0063 (0.0033) | 0.055 | 0.150 |
| **Men** | 0.0111 (0.0050) | **0.028** | — | 0.0127 (0.0063) | **0.043** | — | 0.0107 (0.0038) | **0.005** | — | 0.0114 (0.0048) | **0.016** | — |
| **Women** | 0.0085 (0.0044) | 0.055 | — | 0.0029 (0.0058) | 0.614 | — | 0.0055 (0.0035) | 0.114 | — | 0.0022 (0.0045) | 0.632 | — |
| ***PRL*** | **rs4712652** | **All** | -0.0011 (0.0045) | 0.813 | 0.079 | 0.0006 (0.0057) | 0.911 | **0.019** | 0.0001 (0.0035) | 0.986 | 0.090 | 0.0034 (0.0045) | 0.455 | **0.035** |
| **Men** | 0.0064 (0.0068) | 0.350 | — | 0.0147 (0.0084) | 0.082 | — | 0.0059 (0.0054) | 0.272 | — | 0.0135 (0.0067) | **0.042** | — |
| **Women** | -0.0080 (0.0059) | 0.179 | — | -0.0113 (0.0078) | 0.148 | — | -0.0050 (0.0047) | 0.286 | — | -0.0048 (0.0061) | 0.434 | — |
| ***MTCH2*** | **rs10838738** | **All** | 0.0016 (0.0033) | 0.631 | **0.013** | 0.0023 (0.0042) | 0.585 | 0.177 | 0.0033 (0.0026) | 0.198 | 0.062 | 0.0034 (0.0033) | 0.306 | 0.968 |
| **Men** | -0.0071 (0.0050) | 0.153 | — | -0.0036 (0.0062) | 0.557 | — | -0.0017 (0.0039) | 0.656 | — | 0.0039 (0.0048) | 0.421 | — |
| **Women** | 0.0093 (0.0043) | **0.032** | — | 0.0076 (0.0057) | 0.180 | — | 0.0079 (0.0034) | **0.021** | — | 0.0035 (0.0045) | 0.432 | — |
| ***FTO*** | **rs8050136** | **All** | 0.0074 (0.0047) | 0.111 | 0.185 | 0.0041 (0.0060) | 0.492 | 0.449 | 0.0094 (0.0036) | **0.010** | **0.049** | 0.0086 (0.0046) | 0.062 | 0.259 |
| **Men** | 0.0142 (0.0071) | **0.046** | — | 0.0090 (0.0089) | 0.310 | — | 0.0180 (0.0054) | **9.59×10-4** | — | 0.0149 (0.0068) | **0.028** | — |
| **Women** | 0.0015 (0.0061) | 0.810 | — | -0.0003 (0.0080) | 0.966 | — | 0.0035 (0.0048) | 0.470 | — | 0.0042 (0.0063) | 0.499 | — |
| ***MC4R*** | **rs12970134** | **All** | 0.0061 (0.0039) | 0.117 | 0.090 | 0.0045 (0.0049) | 0.365 | 0.104 | 0.0035 (0.0030) | 0.248 | 0.301 | -0.0001 (0.0038) | 0.971 | 0.095 |
| **Men** | 0.0124 (0.0057) | **0.031** | — | 0.0126 (0.0072) | 0.079 | — | 0.0063 (0.0045) | 0.157 | — | 0.0065 (0.0055) | 0.241 | — |
| **Women** | -0.0003 (0.0052) | 0.954 | — | -0.0033 (0.0068) | 0.631 | — | 0.0003 (0.0040) | 0.937 | — | -0.0062 (0.0052) | 0.238 | — |

Abbreviations: BMI, body mass index; SE, standard error; SNP, single nucleotide polymorphism; WC, waist circumference.

In men or women populations, β coefficients and SEs were determined for the minor allele of SNP using multivariate linear regression under an additive assumption adjusted for age. In the sex-combined population, β coefficients and SEs were determined for the minor allele of SNP using multivariate linear regression under an additive assumption adjusted for age and sex. The interaction term (SNP×sex) was further included in the generalized linear models to assess the interaction between SNP and sex. All non-Gaussian distributed quantitative traits were natural logarithmically transformed to normalize distributions.

*P* values <0.05 are shown in the table and are denoted in bold. None of the *P* values was <2.31 × 10-4 after Bonferroni correction (0.05/216).

**Supplementary table 4**. Associations of the genetic risk score with waist circumference and body mass index in untreated and treated type 2 diabetes.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Traits** | **Population** |  | **Type 2 diabetes** | **Type 2 diabetes (30≤ age <60)** | **Type 2 diabetes (age ≥60)** |
| **All****(n=4,036)** | **Men****(n=1,765)** | **Women****(n=2,271)** | **All****(n=2,480)** | **Men****(n=1,111)** | **Women****(n=1,369)** | **All****(n=1,451)** | **Men****(n=590)** | **Women****(n=861)** |
| **WC** | **GRS groups** |  |  |  |  |  |  |  |  |  |  |
|  | **T1 (9~18)** | **WC, cm** | 88.00 (82.00, 94.00) | 90.00 (84.00, 96.00) | 86.00 (80.00, 92.00) | 88.00 (81.50, 94.00) | 90.00 (84.00, 97.00) | 86.00 (79.00, 90.00)b | 89.00 (82.00, 95.00) | 90.00 (84.00, 95.00) | 88.00 (80.00, 94.00)b |
|  | **T2 (19~20)** | **WC, cm** | 88.00 (81.00, 95.00) | 91.00 (86.00, 98.00) | 85.00 (79.00, 92.00) | 88.00 (81.00, 94.00) | 91.00 (86.00, 98.00)a | 84.00 (78.00, 91.00)b | 89.00 (82.00, 95.00) | 91.00 (85.00, 96.00) | 87.50 (82.00, 93.00)b |
|  | **T3 (21~27)** | **WC, cm** | 89.00 (82.00, 96.00) | 92.00 (86.00, 99.00) | 86.00 (80.00, 93.00) | 89.00 (82.00, 95.00)a | 92.00 (87.00, 98.00)a | 85.00 (80.00, 92.00)b | 89.00 (81.25, 95.90) | 91.00 (85.00, 98.00) | 87.00 (80.00, 94.00)b |
|  | **GRS (increased by per allele)** | **β (SE)** | 0.0023 (0.0009) | 0.0046 (0.0014) | 0.0006 (0.0012) | 0.0019 (0.0009) | 0.0037 (0.0013) | 0.0006 (0.0012) | 0.0002 (0.0012) | 0.0023 (0.0019) | -0.0011 (0.0015) |
|  | ***P*** | **0.013** | **8.76×10-4** | 0.596 | **0.033** | **0.005** | 0.611 | 0.842 | 0.230 | 0.497 |
|  | ***P*GRS×sex** | **0.024** | — | — | **0.017** | — | — | 0.137 | — | — |
| **BMI** | **GRS groups** |  |  |  |  |  |  |  |  |  |  |
|  | **T1 (9~18)** | **BMI, kg/m2** | 25.85 (23.59, 28.40) | 25.85 (23.62, 28.55) | 25.88 (23.53, 28.34) | 25.81 (23.73, 28.28) | 25.87 (23.94, 28.35) | 25.79 (23.53, 28.24) | 25.56 (23.23, 27.83) | 25.17 (23.24, 27.31) | 25.88 (23.07, 28.12) |
|  | **T2 (19~20)** | **BMI, kg/m2** | 25.71 (23.50, 28.33) | 26.37 (23.99, 28.74) | 25.39 (23.12, 27.97) | 25.67 (23.41, 28.20) | 26.42 (24.06, 28.54) | 25.25 (22.87, 27.89)b | 25.45 (23.21, 27.64) | 25.51 (23.05, 27.66) | 25.28 (23.55, 27.51) |
|  | **T3 (21~27)** | **BMI, kg/m2** | 26.35 (24.02, 28.97) | 26.51 (24.35, 29.06) | 26.14 (23.73, 28.84) | 26.00 (23.84, 28.72) | 26.30 (24.39, 28.82) | 25.78 (23.59, 28.55) | 25.70 (23.02, 28.26) | 25.71 (23.13, 28.48) | 25.68 (23.01, 28.13) |
|  | **GRS (increased by per allele)** | **β (SE)** | 0.0035 (0.0012) | 0.0057 (0.0017) | 0.0020 (0.0016) | 0.0018 (0.0011) | 0.0033 (0.0016) | 0.0007 (0.0015) | 0.0004 (0.0015) | 0.0015 (0.0024) | -0.0003 (0.0020) |
|  | ***P*** | **0.002** | **9.29×10-4** | 0.203 | 0.112 | **0.043** | 0.656 | 0.800 | 0.537 | 0.882 |
|  | ***P*GRS×sex** | 0.103 | — | — | **0.046** | — | — | 0.656 | — | — |

Abbreviations: BMI, body mass index; GRS, genetic risk score; IQR, interquartile range; SE, standard error; T, tertile; WC, waist circumference.

Data of different GRS groups are shown as median (IQR).

In men or women populations, β coefficients and SEs were determined for the GRS using multivariate linear regression adjusted for age. In sex-combined population, β coefficients and SEs were determined for the GRS using multivariate linear regression adjusted for age and sex. The interaction term (GRS×sex) was further included in the generalized linear models to assess the interaction between GRS and sex. Prior to the comparisons of clinical characteristics, all non-Gaussian distributed quantitative traits were natural logarithmically transformed to normalize distributions.

a, different compared to the T1 group within the same population; b, different compared to men within the same GRS subgroup.

*P* values <0.05 are denoted in bold. *P* values <2.78 × 10-3 which were statistically significant after Bonferroni correction (0.05/18) are denoted in bold and underlined.

**Supplementary table 5.** Associations of single nucleotide polymorphisms with risk for abdominal obesity and general obesity.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Gene** | **SNP** | **Population** | **Treatment naïve type 2 diabetes****(n=2,555)** | **Type 2 diabetes****(n=4,036)** |
| **Abdominal obesity** | **General obesity** | **Abdominal obesity** | **General obesity** |
| **OR (95%CI)** | ***P*** | ***P*SNP×sex** | **OR (95%CI)** | ***P*** | ***P*SNP×sex** | **OR (95%CI)** | ***P*** | ***P*SNP×sex** | **OR (95%CI)** | ***P*** | ***P*SNP×sex** |
| ***TMEM18*** | **rs7561317** | **All** | 1.36 (1.12,1.65) | **0.002** | 0.588 | 1.24 (1.02,1.50) | **0.033** | 0.701 | 1.33 (1.14,1.55) | **2.79×10-4** | 0.381 | 1.19 (1.01,1.40) | **0.034** | 0.531 |
| **Men** | 1.30 (0.97,1.72) | 0.075 | — | 1.20 (0.90,1.60) | 0.221 | — | 1.24 (0.99,1.56) | 0.066 | — | 1.13 (0.89,1.45) | 0.315 | — |
| **Women** | 1.42 (1.09,1.84) | **0.008** | — | 1.27 (0.97,1.66) | 0.079 | — | 1.41 (1.15,1.74) | **0.001** | — | 1.25 (1.00,1.55) | 0.051 | — |
| ***GNPDA2*** | **rs10938397** | **All** | 1.16 (1.03,1.31) | **0.014** | 0.937 | 1.03 (0.90,1.17) | 0.679 | 0.511 | 1.15 (1.05,1.27) | **0.003** | 0.321 | 1.06 (0.96,1.18) | 0.245 | 0.433 |
| **Men** | 1.16 (0.97,1.39) | 0.099 | — | 1.08 (0.89,1.30) | 0.452 | — | 1.21 (1.05,1.40) | **0.008** | — | 1.11 (0.95,1.30) | 0.179 | — |
| **Women** | 1.16 (0.99,1.36) | 0.066 | — | 0.99 (0.83,1.18) | 0.911 | — | 1.11 (0.98,1.26) | 0.113 | — | 1.03 (0.89,1.18) | 0.732 | — |
| ***TFAP2B*** | **rs987237** | **All** | 1.11 (0.96,1.29) | 0.166 | 0.561 | 1.19 (1.02,1.39) | **0.032** | 0.833 | 1.11 (0.98,1.25) | 0.093 | 0.874 | 1.17 (1.03,1.33) | **0.016** | 0.706 |
| **Men** | 1.05 (0.84,1.32) | 0.656 | — | 1.17 (0.92,1.48) | 0.206 | — | 1.09 (0.91,1.31) | 0.333 | — | 1.14 (0.94,1.38) | 0.195 | — |
| **Women** | 1.16 (0.95,1.41) | 0.147 | — | 1.21 (0.98,1.49) | 0.079 | — | 1.12 (0.95,1.31) | 0.165 | — | 1.20 (1.01,1.42) | **0.040** | — |
| ***BDNF*** | **rs925946** | **All** | 1.25 (0.97,1.62) | 0.089 | 0.557 | 1.40 (1.08,1.82) | **0.012** | 0.751 | 1.18 (0.96,1.44) | 0.119 | 0.391 | 1.23 (0.99,1.53) | 0.063 | 0.483 |
| **Men** | 1.32 (0.90,1.94) | 0.154 | — | 1.44 (0.98,2.11) | 0.062 | — | 1.29 (0.94,1.76) | 0.110 | — | 1.33 (0.96,1.84) | 0.083 | — |
| **Women** | 1.17 (0.82,1.67) | 0.379 | — | 1.35 (0.94,1.94) | 0.110 | — | 1.09 (0.83,1.43) | 0.534 | — | 1.14 (0.85,1.54) | 0.370 | — |
| ***MTCH2*** | **rs10838738** | **All** | 1.06 (0.94,1.19) | 0.327 | **0.028** | 1.06 (0.93,1.20) | 0.367 | 0.211 | 1.12 (1.02,1.23) | **0.021** | 0.078 | 1.02 (0.92,1.13) | 0.764 | 0.995 |
| **Men** | 0.92 (0.77,1.10) | 0.352 | — | 0.97 (0.81,1.18) | 0.788 | — | 1.02 (0.89,1.18) | 0.784 | — | 1.02 (0.87,1.20) | 0.788 | — |
| **Women** | 1.20 (1.03,1.40) | **0.023** | — | 1.14 (0.97,1.35) | 0.120 | — | 1.21 (1.07,1.37) | **0.003** | — | 1.02 (0.89,1.17) | 0.790 | — |
| ***FTO*** | **rs8050136** | **All** | 1.08 (0.91,1.27) | 0.372 | 0.060 | 1.15 (0.96,1.37) | 0.123 | 0.113 | 1.08 (0.95,1.23) | 0.259 | **0.016** | 1.16 (1.01,1.34) | **0.039** | 0.211 |
| **Men** | 1.30 (1.00,1.68) | **0.049** | — | 1.34 (1.03,1.74) | **0.027** | — | 1.31 (1.07,1.60) | **0.009** | — | 1.29 (1.05,1.60) | **0.018** | — |
| **Women** | 0.93 (0.75,1.16) | 0.540 | — | 1.00 (0.79,1.28) | 0.985 | — | 0.94 (0.79,1.12) | 0.497 | — | 1.07 (0.88,1.30) | 0.475 | — |
| ***MC4R*** | **rs12970134** | **All** | 1.16 (1.01,1.33) | **0.034** | 0.201 | 1.16 (1.00,1.34) | 0.053 | 0.696 | 1.09 (0.98,1.21) | 0.128 | 0.223 | 1.04 (0.93,1.18) | 0.483 | 0.345 |
| **Men** | 1.27 (1.03,1.56) | **0.024** | — | 1.18 (0.96,1.47) | 0.120 | — | 1.16 (0.99,1.37) | 0.069 | — | 1.11 (0.93,1.32) | 0.268 | — |
| **Women** | 1.07 (0.89,1.29) | 0.496 | — | 1.12 (0.91,1.37) | 0.275 | — | 1.02 (0.88,1.18) | 0.791 | — | 0.99 (0.84,1.16) | 0.859 | — |

Abbreviations: CI, confidence interval; OR, odds ratio; SNP, single nucleotide polymorphism.

In men or women populations, ORs and 95% CIs were determined for the minor allele of SNP using logistic regression under an additive assumption adjusted for age. In sex-combined population, ORs and 95% CIs were determined for the minor allele of SNP using logistic regression under an additive assumption adjusted for age and sex. The interaction term (SNP×sex) was further included in the logistic models to assess the interaction between SNP and sex.

*P* values <0.05 are shown in the table and are denoted in bold. None of the *P* values was <2.31 × 10-4 after Bonferroni correction (0.05/216).

**Supplementary table 6.** Associations of the genetic risk score with abdominal and general obesity in untreated and treated type 2 diabetes.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Traits** | **Population** |  | **Type 2 diabetes** | **Type 2 diabetes (30≤ age <60)** | **Type 2 diabetes (age ≥60)** |
| **All****(n=4,036)** | **Men****(n=1,765)** | **Women****(n=2,271)** | **All****(n=2,480)** | **Men****(n=1,111)** | **Women****(n=1,369)** | **All****(n=1,451)** | **Men****(n=590)** | **Women****(n=861)** |
| **Abdominal obesity** | **GRS groups** |  |  |  |  |  |  |  |  |  |  |
|  | **T1 (9~18)** | **As reference** | ref. | ref. | ref. | ref. | ref. | ref. | ref. | ref. | ref. |
|  | **T2 (19~20)** | **OR (95%CI)** | 0.99 (0.85,1.15) | 1.23 (0.98,1.54) | 0.84 (0.68,1.02) | 0.97 (0.80,1.17) | 1.32 (0.99,1.76) | 0.75 (0.58,0.98) | 1.01 (0.78,1.30) | 1.09 (0.74,1.61) | 0.95 (0.68,1.33) |
|  | ***P*** | 0.864 | 0.076 | 0.081 | 0.751 | 0.060 | **0.033** | 0.946 | 0.650 | 0.785 |
|  | **T3 (21~27)** | **OR (95%CI)** | 1.07 (0.92,1.24) | 1.39 (1.11,1.75) | 0.87 (0.71,1.06) | 1.15 (0.95,1.40) | 1.54 (1.15,2.06) | 0.92 (0.71,1.20) | 0.92 (0.71,1.18) | 1.15 (0.77,1.71) | 0.78 (0.56,1.09) |
|  | ***P*** | 0.413 | **0.005** | 0.169 | 0.147 | **0.004** | 0.542 | 0.497 | 0.496 | 0.148 |
|  | **GRS (increased by per allele)** | **OR (95%CI)** | 1.01 (0.99,1.04) | 1.06 (1.02,1.10) | 0.98 (0.95,1.01) | 1.03 (0.99, 1.06) | 1.08 (1.03, 1.13) | 0.99 (0.95, 1.03) | 0.98 (0.94, 1.03) | 1.01 (0.94, 1.09) | 0.96 (0.91, 1.02) |
|  | ***P*** | 0.371 | **0.006** | 0.243 | 0.100 | **0.002** | 0.672 | 0.431 | 0.758 | 0.212 |
|  | ***P*GRS×sex** | **0.004** | — | — | **0.008** | — | — | 0.309 | — | — |
| **General obesity** | **GRS groups** |  |  |  |  |  |  |  |  |  |  |
|  | **T1 (9~18)** | **As reference** | ref. | ref. | ref. | ref. | ref. | ref. | ref. | ref. | ref. |
|  | **T2 (19~20)** | **OR (95%CI)** | 0.96 (0.81,1.13) | 1.06 (0.82,1.37) | 0.89 (0.70,1.11) | 0.99 (0.80,1.22) | 1.09 (0.80,1.50) | 0.90 (0.67,1.21) | 0.92 (0.69,1.24) | 1.12 (0.70,1.80) | 0.82 (0.56,1.20) |
|  | ***P*** | 0.601 | 0.670 | 0.299 | 0.899 | 0.574 | 0.481 | 0.603 | 0.644 | 0.314 |
|  | **T3 (21~27)** | **OR (95%CI)** | 1.20 (1.02,1.42) | 1.33 (1.04,1.71) | 1.12 (0.89,1.40) | 1.20 (0.97,1.48) | 1.25 (0.92,1.71) | 1.16 (0.87,1.54) | 1.20 (0.90,1.60) | 1.60 (1.00, 2.54) | 1.00 (0.69,1.45) |
|  | ***P*** | **0.029** | **0.026** | 0.340 | 0.092 | 0.152 | 0.310 | 0.218 | **0.049** | 0.997 |
|  | **GRS (increased by per allele)** | **OR (95%CI)** | 1.02 (0.99,1.05) | 1.05 (1.01,1.10) | 1.00 (0.97,1.04) | 1.02 (0.99, 1.06) | 1.04 (0.98, 1.09) | 1.01 (0.96, 1.06) | 1.02 (0.97, 1.08) | 1.09 (1.00, 1.19) | 0.99 (0.93, 1.05) |
|  | ***P*** | 0.117 | **0.029** | 0.849 | 0.232 | 0.179 | 0.654 | 0.368 | **0.048** | 0.697 |
| 　 | ***P*GRS×sex** | 0.120 | — | — | 0.458 | — | — | 0.069 | — | — |

Abbreviations: CI, confidence interval; GRS, genetic risk score; OR, odds ratio; T, tertile.

In men or women populations, ORs and 95% CIs were determined for the GRS or the T3 and T2 groups compared to the T1 group, using logistic regression adjusted for age. In sex-combined population, ORs and 95% CIs were determined for the GRS or the T3 and T2 groups compared to the T1 group, using logistic regression adjusted for age and sex. The interaction term (GRS×sex) was further included in the logistic models to assess the interaction between GRS and sex.

*P* values <0.05 are denoted in bold. None of the *P* values was <1.39 × 10-3 after Bonferroni correction (0.05/36).



**Supplementary figure 1.** The distribution of genetic risk score in the treatment naïve type 2 diabetes of Chinese ancestry.

GRS, genetic risk score.